## REMARKS

### *Status of the Claims*

Claims 1, 9-12, and 20-35 are pending. Claims 1, 9-12, 20-21, and 30-35 are pending and under examination on the merits. Claims 22-29 are also pending and have been withdrawn from consideration. Claims 36 and 37 have been added. Upon entry of this amendment, claims 1, 9-12, 20-35 remain pending and claims 1, 9-12, 20-21, and 30-37 will be pending and under examination.

### *Summary of the Amendment*

Claims 36 and 37 have been added to recite that the composition is effective to inhibit a Th1 T-cell immune response is effective to decrease interferon-γ levels. Support for new claims 36 and 37 can be found throughout the application and the examples. In response to the Notice of Non-Complaint amendment the claim identifier for claim 21 has been changed to "Previously Presented." No new matter has been added.

### *Brief Summary of the Invention*

The pending claims are directed to compositions that comprise 1) a nucleic acid eukaryote cell expression carrier and 2) a polypeptide and that are effective to ***inhibit***, rather than enhance or induce, a Th1 T-cell immune response.

### *Claim Rejections Under 35 U.S.C. § 112*

#### *Written Description*

Claims 1, 9-12, 19-21, and 30-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office alleges that the application contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the presently claimed invention. The Office alleges that the specification does not disclose any example where a composition is shown to be a Th1 T-cell

inhibitor. The Office alleges that the combination of the protein antigen and a nucleic acid expression vector expressing the same antigen "elicited the same level of antibodies as the other treatments." (Office Action, page 4). The Office alleges that the combination "led to T-cell expansion in every case." The Office alleges that "there were no tests performed that looked specifically at Th1 cells or any specific type of Th1 cell activity." (Office Action, page 4). The Office alleges that "therefore, the specification lacks description of any composition that meets the limitations of the claims." Because the specification describes the presently claimed subject matter and shows Applicants to be in possession of the presently claimed invention through a working example Applicants respectfully disagree.

The presently claimed invention and the specification satisfy the written description. The written description requirement is satisfied because the specification explicitly describes the claimed invention and the specification provides a working example of the presently claimed invention. The Office's allegations to the contrary are based on mischaracterizations of the present application, and, therefore, in view of the foregoing, the Office has failed to demonstrate that one of skilled in the art would not have understood that Applicants were in possession of the invention at the time the present application was filed.

The specification and claims satisfy the written description requirement because the present application provides examples of compositions that fall within the scope of the claim that act as Th1 T-cell response inhibitors. Applicants note that the presently claimed invention is unrelated to antibody production. The Office's characterization that the examples provided in the specification "elicited the same level of antibodies as the other treatments" is irrelevant to the presently claimed invention. For example, the specification of the present application states:

> The T-cell immune response inhibitor in the present invention may stimulate the organism to produce the normal specific antibody immune response and inhibit the specific cellular immune response, especially the Th1 immune response. (Paragraph 68 of the Published Application)

The analysis that the Office has used to determine whether or not the claims and specification satisfy the written description requirement is flawed because Applicants have never claimed or

stated that the antibody response would be different. Rather the compositions are for inhibition of the Th1 T-cell immune response, which is a cellular response and not an antibody response.

With respect to the Th1 T-cell immune response, Figure 11 of the present application shows that the production of IFN-γ is decreased in the presence of the inhibitors of the presently claimed invention. In paragraph 0065 of the published application, the specification states that when mice are administered the "T-cell immune response inhibitor the animal's …IFN-γ levels decrease." The Office admits that interferon-γ is the "signature cytokine of Th1 cells." (Office Action, page 5, line 14). Therefore, a decrease in IFN-γ levels as was seen using a composition within the scope of the presently claimed invention demonstrates that Applicants were in possession of a composition for inhibiting a Th1 T-cell immune response.

The presently claimed invention also satisfies the written description requirement because the specification provides structural characteristics that allows one of skill in the art to immediately envisage the claimed composition. Claim 1 states that the composition comprises a nucleic acid eukaryote cell expression carrier encoding a targeted antigen; and the targeted antigen polypeptide that is encoded by said nucleic acid eukaryote cell expression carrier encoding a targeted antigen, wherein ratio of the nucleic acid eukaryote cell expression carrier to the antigen polypeptide is selected from the group consisting of 5:1 (w/w), from 2:1 to 10:1(w/w), from 1:5 to 5:1(w/w), and from 1:2 to 1:10(w/w). The claim and the specification specifically discloses the structural features of the claimed composition. The written description requirement requires nothing more. The Office's written description rejection is tantamount to an enablement rejection, which is analyzed under a different set of criteria and is addressed by Applicants below to respond to the Office's enablement rejection. The claims and the specification clearly set forth the structure of the composition, which satisfies the written description requirement.

Accordingly, Applicants have shown that they were in possession of the presently claimed invention because Applicants have provided the specific structure of the composition and disclosed working examples.

The Federal Circuit has recently described the requirements of the written description requirement. The presently claimed invention satisfies the written description requirement because the specification demonstrates "that the applicant[s] ha[ve] made a generic invention that achieves the claimed result and do[es] so by showing that the applicant[s] [have] invented species sufficient to support a claim to the ... defined genus." *Ariad Pharmaceuticals v. Eli Lilly & Co.*, (Fed. Cir. Docket No. 2008-1248, March 22, 2010, at *20). The presently claimed specification describes more than just a function, it describes the structure of the presently claimed invention. The presently claimed invention and the specification defines the structure of the composition. Contrary to the Office's conclusion the specification provides an example of a composition that falls within the scope of the claim and the presently claimed invention is described based on the components (structure) of the composition. Since the compositions are described by a specific structure, one of skill in the art could immediately envisage the structure of the presently claimed composition. There is no requirement that the specification describe every possible antigen that could be used as the basis of the composition. The written description requirement also does not require Applicants to provide working examples of every species. Applicants respectfully assert that contrary to the Office's rejection there is no requirement, and there has never been a requirement, under 35 U.S.C. § 112, first paragraph, that the claims be limited to what is only disclosed or exemplified. The Office's rejection seems to be conflating the requirements for a sufficient written description with that of an enabling disclosure. The present application satisfies all the requirements under 35 U.S.C. § 112.

As opposed to the Office's characterization of what is required, a sufficient description of a genus requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus. *Ariad* at *21. Here, Applicants have done both. Applicants have disclosed a sufficient number of species and described the common structural features of the presently claimed invention. Specifically, the structure of the composition is a nucleic acid eukaryote cell expression carrier encoding a targeted antigen; and

the targeted antigen polypeptide that is encoded by said nucleic acid eukaryote cell expression carrier encoding a targeted antigen, wherein ratio of the nucleic acid eukaryote cell expression carrier to the antigen polypeptide is selected from the group consisting of 5:1 (w/w), from 2:1 to 10:1(w/w), from 1:5 to 5:1(w/w), and from 1:2 to 1:10(w/w).

The Federal Circuit also stated that to determine whether the present application satisfies the written description requirement "requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* at *24. Satisfying the written description requirement "does not demand either examples or an actual reduction to practice." *Id.* at *25. Instead "a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Id.* Here, Applicants have provided specific working examples and Applicants have provided a constructive and actual reduction to practice that definitively identifies the claimed invention and shows that Applicants were in possession of the presently claimed invention at the time the application was filed.

The Federal Circuit has also overturned a similar rejection to the one presented here by the Office. The present rejection suggests that Applicants have not shown possession because they have not exemplified every composition with every possible antigen. Applicants' invention is not unlike that in *Capon v. Eshhar*, 418 F.3d 1349, 1359-1360, (Fed. Cir. 2005). In Capon, the claims recited chimeric DNAs (or genes) comprising DNA encoding, for example, a single chain Fv domain of a specific antibody and the transmembrane and cytoplasmic domain of an endogenous protein. *Id.* at 1352-1353. The Board had rejected such claims for lack of written description, arguing that novel genetic material was being described in terms of the functional characteristics of the protein encoded. Id. at 1354-1355. The Board, relying upon much of the same precedent relied upon by the Office in rejecting the presently claimed invention, was requiring the complete sequence or disclosure of the proteins to be included within the scope of the claim. *Id.* The Federal Circuit overturned the Board's rejection, observing that none of the cases relied upon by the Board required a re-description of what was already known. *Id.*, at 1357-1358. In the present case, as in Capon, the Applicants should not be required to re-describe

what is already known. Applicants are not required to list every possible antigen that could be used.

The Office has attempted to argue that the claims require more description than what is contained in the specification based on an unsubstantiated conclusion that the specification does not includes working examples of compositions that fall within the scope of claim 1. Applicants respectfully assert that a complete reading of the specification shows that the Office's allegation is completely inaccurate. As described above, the specification provides a working example of a composition that is a Th1 T-cell inhibitor. Therefore, the Office's conclusion is wrong. Applicants respectfully assert that the rejection cannot be maintained because the facts used by the Office to support the rejection are not correct.

The Office appears to also argue that the prior art does not support the claimed invention, and, therefore, the claims are not supported by a sufficient written description. Applicants respectfully disagree. The references cited by the Office do not support a conclusion that the claims are not supported by a sufficient written description. The uncertainty allegation that the Office uses is more suitable for an enablement rejection, not for supporting a written description rejection. However, even if the use of the references were proper, the presently claimed invention provides sufficient structures of the compositions such that the one of skill in the art would be able to immediately envisage and recognize the claimed compositions and that Applicants were in possession of the presently claimed invention at the time the application was filed. Additionally, as discussed above, the specification provides a working example of the presently claimed invention that demonstrates that Applicants were in possession at the time the application was filed.

Complexity and predictability with respect to the written description requirement relates to whether the structure of an element of the claimed invention can be envisaged or recognized at the time the application was filed. For example in *Ariad*, the claims were directed to "A method for reducing, in eukaryotic cells, the level of expression of genes which are activated by extracellular influences which induce NF-κB-mediated intracellular signaling, the method

comprising reducing NF-κB activity in the cells such that expression of said genes is reduced carried out on human cells." *Ariad* at *3. In *Ariad*, the Federal Circuit found that these claims did not satisfy the written description requirement because the specification did not describe how the method would be performed. That is, in the patent at issue in *Ariad* there were no examples of molecules or compounds that could be used in the claimed method. Additionally, the court found that this area of research was unpredictable due to the novelty of NF- κB at the time the application was filed. Therefore, one of skill in the art would not have been able to immediately envisage or recognize the molecules that could be used to reduce NF-κB activity. See *Id.* at *37, 38.

In contrast to the facts in *Ariad*, the present specification provide examples of concrete and non-hypothetical compositions that are Th1 T-cell inhibitors. These examples fall within the scope of the presently claimed invention. There is nothing hypothetical about the example provided in the application. Therefore, unlike the claimed invention in *Ariad*, the presently claimed invention satisfies the written description requirement.

The Office has failed to provide any reasonable argument to rebut the only reasonable conclusion that the present application satisfies the written description requirement. If the Office maintains the present rejection, Applicants respectfully request that the Office explain why one of skill in the art could not visualize or recognize a composition as it is claimed and with the description of a working example understand that Applicants were in possession of the presently claimed invention.

Applicants have also added new claims 36 and 37, which are also adequately described by the present specification. The specification states that the presently claimed compositions decrease interferon-γ levels and that these levels are decreased in a subject when compared to a subject that has not been treated with the presently claimed composition and is exposed to the antigen.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph as allegedly lacking sufficient written description be withdrawn.

***Claim Rejections Under 35 U.S.C. § 112***

***Enablement***

Claims 1, 9-12, 19-21, and 30-35 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. Applicants respectfully disagree.

The presently claimed invention is enabled because one of skill in the art following the examples and the specification would be able to make and use the presently claimed invention without undue experimentation. The claims are also enabled because the Office has failed to raise a reasonable question as to the enablement of the presently claimed invention. The Office's conclusion that the presently claims invention is not enabled is based on an erroneous understanding of the claims and the specification. Therefore, for these reasons and as discussed below the presently claimed invention is enabled.

The presently claimed invention is enabled. The Office is respectfully reminded that to support an enablement rejection sufficient evidence to question the enablement must be provided. A specification enables an invention if it provides guidance and one of skill the art would not have to perform undue experimentation to practice the invention. The Office has not articulated a reason "to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi* , 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office has failed to provide any evidence to support any reason as to why the presently claimed invention is not enabled. The Office's unsubstantiated allegation that the claims are not enabled based on unsubstantiated claims of uncertainty cannot be maintained. Without sufficient evidence to raise a doubt regarding the enablement of the pending claims the Office must withdraw the enablement rejection.

Regardless of the Office's failure to carry its burden, one of skill in the art can make and use the presently claimed invention without undue experimentation by following the teachings of

the present specification. The present specification provides a working example of a composition that is effective to inhibit a Th1 T-cell response. As discussed above in the context of the written description rejection, the specification provides an example of a composition that decreases a Th1 response (*e.g.* interferon-γ levels). As admitted by the Office, interferon- γ is the "signature cytokine of Th1 cells." (Office Action, page 5, line 14). Therefore, the decrease in the "signature cytokine of Th1 cells" demonstrates that the Th1 T-cell response is being inhibited. The Office's observation that the antibody levels in each experiment are increased is irrelevant to the presently claimed invention. The composition of the presently claimed invention is not directed to a composition that is effective to inhibit an antibody response. The composition is for the inhibition of a Th1 T-cell response, which is not related to antibody production. Therefore, the facts that the Office's enablement rejection are based upon are erroneous and do not support the Office's conclusion that the claims are not enabled.

In addition to the Office failing to show that the claims are not enabled, Applicants enclose herewith a declaration describing compositions that are effective to inhibit a Th1 T-cell response as is claimed and fall within the scope of the presently claimed invention.[1] The declaration by Dr. Wang states that he has made and used compositions that fall within the scope of the claims that inhibit a Th1 T-cell immune response for Flea Antigen protein, zona pellucida 3 protein, insulin, Derp1 protein, and OVA protein antigen. (Declaration, paragraphs 3-9). The data includes data that has been published in a peer-reviewed scientific publication. (Declaration Paragraph 3 and Exhibit 1). The declaration states that a "Th1 T-cell immune response can be measured by measuring T-cell proliferation." (Declaration, paragraph 4). With the antigens tested a composition that is within the scope of the claim was able to inhibit a Th1 T-cell immune response. Accordingly, the claims are enabled because one of skill in the art can make and use the composition without undue experimentation.

[1] The executed declaration was submitted on July 6, 2010.

Accordingly, the claims are enabled for the reasons discussed above. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

***Double Patenting***

Claims 1-6, 10-12, 20, 30-35 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 10, and 11 of co-pending application No. 11/644,435. The Office alleges that although the claims are not identical they are not patentably distinct from each other because the claims of co-pending application number 11/644,435 are drawn to a composition comprising a eukaryotic cell expression vector containing nucleotide sequences encoding an allergenic protein and the protein or polypeptide that comprises an antigenic epitope of said protein. The Office alleges that the vector comprises an RSV, CMV, or SV40 promoter and the vector is in the proportion to the protein in a ratio of 1:15 to 5:1. Applicants respectfully assert that the present obviousness-type double patenting rejection should be withdrawn since the all other rejections have been obviated and this is the only remaining rejection. The present application is the earlier filed application. Accordingly, the provisional rejection should be withdrawn and the present application should be allowed to issue.

In view of the foregoing, Applicants respectfully request that the rejection under obviousness-type double patenting be withdrawn.

***Conclusion***

Claims 1, 9-12, 20-21, and 30-37 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7820 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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Attachments:
Declaration by Dr. Bin Wang (Unexecuted Version Submitted June 30, 2010 and Executed Version submitted July 6, 2010)
Declaration Exhibits 1-5 (Submitted June 30, 2010)